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THE ROLE OF CIRCULATING MICROBIAL DNA (CF-MBDNA) AS AN EARLY BIOMARKER OF CHRONIC INFLAMMATION IN LONG-STANDING DIABETES MELLITUS AND ITS ASSOCIATION WITH MICROVASCULAR COMPLICATIONS: A SYSTEMATIC REVIEW

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Abstract

Background: Circulating microbial DNA (cf-mbDNA) and related cell-free DNA (cfDNA) fragments have emerged as novel biomarkers reflecting metabolic stress, inflammation, and vascular injury in diabetes mellitus (DM). This systematic review aimed to synthesize current evidence on their diagnostic potential for detecting chronic inflammation and microvascular complications in long-standing diabetes. Study Purpose/

Objectives: The role of circulating microbial DNA (cf-mbDNA) as an early biomarker of chronic inflammation in long-standing diabetes mellitus and its association with microvascular complications: A systematic review

Methods: Following PRISMA 2020 guidelines, ten peer-reviewed studies published between 2010 and 2025 were systematically analyzed across multiple databases. Eligible studies assessed cfDNA or cf-mbDNA in plasma or serum samples from patients with type 1 or type 2 diabetes, investigating associations with inflammatory and vascular markers.

Results: Across the reviewed literature, cfDNA profiles—such as 5-hydroxymethylcytosine patterns, methylation signatures, and microbial fragments—were consistently associated with endothelial dysfunction, renal impairment, and systemic inflammation. Quantitative models based on cfDNA achieved high diagnostic performance, with reported AUC values exceeding 0.85 for identifying vascular complications. Studies further demonstrated that increased cf-mbDNA and decreased mitochondrial cfDNA were linked to heightened inflammatory activity and metabolic dysfunction.



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Conclusion: Circulating microbial and cell-free DNA biomarkers represent promising noninvasive indicators of chronic inflammation and early microvascular damage in diabetes. They provide mechanistic insight into the interplay between metabolic dysregulation, immune activation, and vascular injury. Standardized detection methods and longitudinal validation are needed to support their integration into clinical practice.

Key Words: circulating microbial DNA, cfDNA, diabetes mellitus, inflammation, microvascular complications, biomarkers, mitochondrial DNA, epigenetics, nephropathy, retinopathy.